Thu Sep 16 09:09:54 2004

Appendix a

\*

The invention relates to a novel human G-coupled receptor (1). (1) and its corresponding polynucleotides are useful for diagnosing, treating or preventing cell proliferative diseases (e.g. lymboma, leukaemia, breast cancer or cirrhosis), neurological disorders (e.g. stroke, Alzheimer's diseases, multiple sclerosis or mental retardation), cardiovascular diseases (e.g. arberoelerosis, angina pectoris or congestive heart failure), gastrointestinal disorders (e.g. dysphagia, indigestion or gastritis), autoimmune/inflammacory disorders (e.g. AIDS, Crohn's disease or systemic lupus erythematosus) or metabolic disorders (e.g. diabetes or parvovirus), AAUS0493-AAUS0515 represent novel human G-coupled receptor amino acid sequences of the invention

Sequence 321 AA;

ö VYLFLCMLSTIDLAASVSTVPKLLAIFWCGAGHISASACLAHMFFIHAFCMMESTVLLAM 128 AFDRYVAICHPLRYATILTDTIIAHIGVAAVVRGSLIMLPCPFFIGRINFCQSHVILHTY 188 180 248 GTCGSHVCVILISYTPALFSFFTHRFGHHVPVHIHILLANVYLLLPPALNPVVYGVKTKQ 308 241 GTCGSHVCVILISYTPALFSFFTHRFGHHVPVHIHILLANVYLLIPPALNPVVYGVKTKQ 300 68 09 121 AFDRYVAICHPLRYATILTDTIIAHIGVAAVVRGSLLMLPCPFLIGRLNRCQSHVILHTY 9 MESPHHIDVDPSVFFLLGIPGLEQFHLWLSLPVCGLGTATIVGNITILVVVATEPVLHKP CEHMAVVKLACGDTRPNRVYGLTAALLVIGVDLFCIGLSYALIAQAVLRLSSHEARSKAL Gaps .; 0 Length 321; Indels 3; 96.0%; Score 1649; DB 5; 98.8%; Pred. No. 2.8e-173; ive 1; Mismatches 3; IRKRVVRVFQSGQGMGIKASE 321 IRKRVVRVFQSGQGMGIKASE Best Local Similarity 96.0 Matches 317; Conservative Similarity 69 61 129 189 249 Query Match 309 301 Ωp à g g à à g дq à à à 윤

Human olfactory and pheromone G protein-coupled receptor #212. AAU95725 standard; protein; 321 AA 02-JUL-2002 (first entry) AAU95725; RESULT 10 AAU95725 ZX4X6X6X6X6X6X6X6X6X6X

Human; olfactory and pheromone G protein coupled; receptor; GPCR;

tranquilizer, antidepressant, neuroleptic; endocrine, anabolic; anorectic; trate; fragrance; food additive; cosmetic; cell migration; sterility; psychotic disorder; neurological disorder; anxiety; schizophrenia; manic depression; depression; axonal growth; menstrual cycle; appetite sexual mctivation; sexual atraction;

Homo sapiens

WO200224726-A2

28-MAR-2002

21-SEP-2001; 2001WO-BE000162.

22-SEP-2000; 2000EP-00870211.

SA (CHEM-) CHEMCOM

Veithen A;

WPI; 2002-330013/36.

N-PSDB; ABK68612

Novel pheromone G-protein coupled receptor and receptor-derived agonists, antagonists or inhibitors useful in food or cosmetic products or in the treatment or prevention of neurological disorders such as anxiety and schizophrenia.

Disclosure; Page 647-648; 833pp; English.

The invention relates to olfactory and Pheromone G-protein coupled receptor (GPCR) or a protein 95% identical to the GPCR, a specific active portion and its encoding polynucleotide. Also included are an agonist, antagonist or inhibitor of the GPCR or the polynucleotide, a vector comprising the polynucleotide, a cell transformed by the vector, a non-thuman mammal comprising a partial or total deletion of the polynucleotide encoding the receptor and screening (detection and possibly, recovering) of compounds which are known or not known to be agonist, antagonists or inhibitors of natural compounds to the GPCR. The receptor-derived agonists, inhibitors or compounds are used as an improvement, elimination or substitution of an existing taste and/or a fragrance of (or in) the food and/or cosmetic products. They can also be used in the preparation of medicament in the treatment and/or prevention of a mammalian disorders, including anxiety, schizophrenia, manic depression, for promoting axonal growth, nerve cell connection and nerve regeneration for modulating male and female connection and nerve regeneration for modulating male and female behaviours, such as stimulation or suppression of appetite, sexual motivation, sexual attraction, aggression and for promoting or suppressing chemical communication between organisms. The present sequence is a human olfactory and pheromone GPCR protein sequence prevention or the treatment by stimulation of several mammalian

Sequence 321 AA;

ó 128 180 188 GTCGSHVCVILISYTPALFSFFTHRFGHHVPVHIHILLANVYLLLPPALNPVVYGVKTKQ 308 GTCGSHVCVILISYTPALFSFFTHRFGHHVPVHIHILLANVYLILLPPALNPVVGVKTKQ 300 9 61 VYLFLCMLSTIDLAASVSTVPKLLAIFWCGAGHISASACLAOMFFIHAFCMMESTVLLAM 9 MESPHHTDVDPSVFFLLGIPGLEQFHLWLSLPVCGLGTATIVGNITILVVVATEPVLHKP 1 MESPNHTDVDPSVFFLLGIPGLEQFHLWLSLPVCGLGTATIVGNITILVVVATEPVLHKP 69 VYLFLCMLSTIDLAASVSTVPKLLAIFWCGAGHISASACLAHMFFIHAFCMMESTVLLLAM AFDRYVAICHPLRYATILIDTIIAHIGVAAVVRGSLLMLPCPFFIGRLNFCQSHVILHTY CEHMAVVKLACGDTRPNRVYGLTAALLVIGVDLFCIGLSYALIAQAVLRLSSHEARSKAL Gaps .. 0 96.0%; Score 1649; DB 5; Length 321; 98.8%; Pred. No. 2.8e-173; ive 1; Mismatches 3; Indels ( Best Local Similarity 98.8 Matches 317; Conservative 129 189 249 Query Match 241 Db ò g g g à g

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RESULT 11
ABR01673
ID ABR016
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ABR01673 standard; protein; 316 AA.

309 IRKRVVRVFOSGOGMGIKASE 329 IRKRVVRVFQSGQGMGIKASE

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301

Appearix UD

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240
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                                                                                                                                                                                                241 HEARSKALGTCGSHVCVILISYTPALFSFFTHRFGHHVPVHIHILLANVYLLLPPALNPV 300
                                                                                                                                                                                                                                       121 ESTVLLAMAFDRYVAICHPLRYATILTDTIIAHIGVAAVVRGSLLMLPCPFLIGRLNFCQ 180
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                                                                  SHVILHTYCEHMAVVKLACGDTRPNRVYGLTAALLVIGVDLFCIGLSYALIAQAVLRLSS
                                                                                                         Human, olfactory receptor; OR; primary scent determination;
secondary scent determination; polypeptide library; odour receptor;
scent profile; scent fingerprint; scent representation.
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24-FEB-2000; 2000US-0184809P.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Human; cytostatic; neuroprotective; immunosuppressant; nootropic; anti-inflammatory; anti-viral; gastrointestinal; cardiovascular; cerebroprotective; G-coupled receptor; cell proliferative disease; lymphoma; leukaemia; breast cancer; cirrhosis; neurological disorder; stroke; Alzheimer's disease; multiple sclerosis; mental retardation; cardiovascular disease; atherosclerosis; angina pectoris; indigestion; congestive heart failure; gastrointestinal disorder; dysphagia; AIDS; gastritis; autoimmune disorder; inflammatory disorder; Crohn's disease; systemic lupus erythematosus; metabolic disorder; diabetes; obesity; viral infection; herpesvirus; parvovirus;
69 VYLFLCMLSTIDLAASVSTVPKLLAIFWCGAGHISASACLAHMFFIHAFCMMESTVLLAM
                                                                  61 VYLFLCMLSTIDLAASVSTVPKLLAIFWCGAGHISASACLAQMFFIHAFCMMESTVLLAM
                                                                                                                                    121 AFDRYVAICHPLRYATILIDTIIAHIGVAAVVRGSLLMLPCPFLIGRLNFCQSHVILHTY
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Human G-coupled receptor (GCREC) protein, Seq ID No 19.
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Au-Young J;
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                                                                                                                                                                                                                                                                                                                  AAU80511 standard; protein; 321
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25-MAY-2000; 2000US-0207476P.
02-JUN-2000; 2000US-0208834P.
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07-JUN-2000; 2000US-0209868P.
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Gandhi AR,
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Kallick DA,
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Claim 1; Page 133-134; 148pp; English

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9 MESPHHTDVDPSVFFLLGIPGLEQFHLWLSLPVCGLGTATIVGNITILVVVATEPVLHKP 68

96.0%; Score 1649; DB 4; Length 321; 98.8%; Pred. No. 2.8e-173; ive 1; Mismatches 3; Indels

Query Match Best Local Similarity 98.81 Matches 317; Conservative

Approx 133

Human; olfactory G-coupled receptor; sensory perception of odourant; odour composition; taste composition AAU85266 standard; protein; 329 AA 22-JUN-2001; 2001WO-US020122 22-JUN-2000; 2000US-0213812P. 13-MAR-2001; 2001US-00804291. Zozulya S, Stryer L; WPI; 2002-083330/11. N-PSDB; ABK37625. (first G-coupled olfactory (SENO-) SENOMYX INC Homo sapiens. 27-DEC-2001, 08-MAY-2002 AAU85266; RESULT 6 AAU85266 

The invention relates to a method of representing sensory perception of one or more odourants. The method comprises: (a) providing a representative class of nolfactory receptors or ligand binding domains (LLBD) of these receptors; (b) measuring values XI to Xn representative of at least one activity of one or more odourants selected from: (i) binding one or more odourants to the LBD of at least one of the nolfactory receptors the one or more odourants; and (ii) blocking at least one of the nolfactory receptors with the one or more odourants; and (iii) blocking at least one of the nolfactory receptors with the one or more odourants; and (c) generating a representation of sensory perception from the values XI to Xn. The design and formulation of odour and taste compositions. AAU85140-AAU85393 represent human olfactory G-coupled receptor amino acid sequences of the Representing sensory perception of one or more odorants for the identification and design of tastes and odors comprises providing representative group of n olfactory receptors. Claim 1; Page 115; 182pp; English

Sequence 329 AA;

o; TEPVI.HKPVYLFLCMLSTIDLAASVSTVPKLLAIFWCGAGHISASACLAHMFFIHAFCMM 120 9 9 MSSTLGHNMESPHHTDVDPSVFFLLGIPGLEQFHLWLSLPVCGLGTATIVGNITILVVVA 0; Gaps Length 329; Indels Score 1691; DB 5; Pred. No. 6.7e-178; 1; Mismatches 3; 98.4**%**; 98.8**%**; Best Local Similarity 98.8 Matches 325; Conservative Local Similarity 61 ò

TEPVLHKPVYLFLCMLSTIDLAASVSTVPKLLAIFWCGAGHISASACLAQMFFIHAFCMM 120

61

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120 120

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Gaps

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Length 329; Indels

98.4%; Score 1691; DB 7; 98.8%; Pred. No. 6.7e-178; live 1; Mismatches 3;

Matches 325; Conservative

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Local Similarity

Query Match

Sequence 329 AA;

1 MSSTLGHNMESPNHTDVDPSVFFLLGIPGLEQFHLWLSLPVCGLGTATIVGNITILVVVA TEPVLHKPVYLFLCMLSTIDLAASVSTVPKLLAIFWCGAGHISASACLAHMFFIHAFCMM TEPVIHKPVYLFLCMLSTIDLAASVSTVPKLLAIFWCGAGHISASACLAQMFFIHAFCMM

61

1 MSSTLGHNMESPHHTDVDPSVFFLLGIPGLEQFHLWLSLPVCGLGTATIVGNITILVVVA

121 ESTVLLAMAFDRXVAICHPLRXATILTDTITAHIGVAAVVRGSLLMLPCPFFIGRLNFCQ 180

240 241 HEARSKALGTCGSHVCVILISYTPALFSFFTHRFGHHVPVHIHILLANVYLLLPPALNPV 300 triphosphate-binding protein coupled receptor (GPCR). A polymucleotide of the invention may have a use in gene therapy. The polymucleotide and polypeptide are useful for preparing a composition for treating a patient in need of increased or suppressed activity or expression of the guanosine triphosphate-binding protein coupled receptor. The protein sequences shown in ADC85549-ADC87617 represent GPCR's of the invention. New polynucleotide, useful for preparing a composition for treating a patient in need of increased or suppressed activity or expression of the guanosine triphosphate-binding protein coupled receptor. HEARSKALGTCGSHVCVILISYTPALFSFFTHRFGHHVPVHIHILLANVYLLLPPALNPV human, GPCR, guanosine triphosphate-binding protein coupled receptor; gene therapy. The invention relates to a novel polynucleotide encoding a guanosine (NAAD-) NAT INST ADVANCED IND SCI & TECHNOLOGY. (ADSC-) CENT ADVANCED SCI & TECHNOLOGY INCUBATIO. 101 VYGVKTKQIRKRVVRVFQSGQGMGIKASE 329 301 VYGVKTKQIRKRVVRVFQSGQGMGIKASE 329 Aburatani SEQ ID NO 798; 28pp; English Æ Human GPCR protein SEQ ID NO:798 ADC86345 standard; protein; 329 18-JUN-2002; 2002EP-00013517. 18-JUN-2001; 2001JP-00246789. Suwa M, Asai K, Akiyama Y, (first entry) WPI; 2003-315783/31. N-PSDB; ADC86344. Homo sapiens EP1270724-A2 01-JAN-2004 32-JAN-2003 241 ADC86345; Claim 2; RESULT 7 ADC86345 a à à

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Mon Aug 30

Hyperchax By

1001 CATATTCACATTCTTTTGGCCAATGTTTATCTGCTTTTGCCACCTGCTCTTAATCCTGTG 1100 The present sequence is one of a number of isolated polynuclectides which encode polypeptides involved in olfactory sensation. The polynuclectides and be used in screening for olfactory agonists and antagonists. The methods allow for the determination of primary scents and the identification of the odour receptors used to detect these primary scents. The methods also enable determination of secondary scents and the identification of combinations of odour receptors that are involved in detecting such secondary scents. This enables the construction of a scent representation (also called a scent fingerprint or scent profile), which receptors are used to re-create and edit scents. Libraries of olfactory composition with the receptors, and can be used for determining the interaction pattern of a composition with the receptors, and can be used for determining differences in the olfactory faculties of different individuals 301 ValTyrGlyValLysThrLysGlnIleArgLysArgValValArgValPheGlnSerGly receptor; New polynucleotides which encode polypeptides involved in olfactory sensation for identifying olfactory agonists and antagonists. Yanai I; Human, olfactory receptor, OR, primary scent determination, secondary scent determination; polypeptide library, odour rescent profile, scent fingerprint, scent representation; ds. 216 G; 290 T; 0 U; 0 Other; Fuchs T, Human olfactory receptor polynucleotide, SEQ ID NO: Glusman G, 321 GlnGlyMetGlyIleLysAlaSerGlu 329 Claim 8; Page 349; 1857pp; English. Lancet D, BP. Sequence 963 BP; 181 A; 276 C; (DIGI-) DIGISCENTS. (YEDA ) YEDA RES & DEV CO LTD 08-OCT-1999; 99US-0158615P. 24-FEB-2000; 2000US-0184809P 06-OCT-2000; 2000WO-US027582 AAH31850 standard; DNA; 963

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New G-protein coupled receptors useful for treating or preventing cell proliferative (e.g. leukemia), neurological (e.g. stroke), cardiovascular or autoimmune/inflammatory disorders.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            The invention relates to a novel human G-coupled receptor (I). (I) and its corresponding polynucleotides are useful for diagnosing, treating or preventing cell proliferative diseases (e.g. lymphoma, leukaemia, breast cancer or cirrhosis), neurological disorders (e.g. stroke, Alzheimer's diseases (e.g. stroke, Alzheimer's diseases (e.g. stroke, Alzheimer's diseases (e.g. stroke, Alzheimer's diseases (e.g. atherosclerosis, angina pectoris or congestive heart failure), gastrointestinal disorders (e.g. dysphagia, indigestion or gastritis), aucoimmune/inflammatory disorders (e.g. AlDS, Crohn's disease or systemic lupus erythematosus) or metabolic disorders (e.g. diabetes or obesity), or viral infections (e.g. infection by herpesvirus or parvovirus). ABK16615-ABK16637 represent novel human G-coupled receptor coding sequences of the invention
                                                                                          Human; cytostatic; neuroprotective; immunosuppressant; nootropic; anti-inflammatory; anti-viral; gastrointeetinal; cardiovascular; cerebroprotective; G-coupled receptor; cell proliferative disease; lymphoma; leukaemia; breast cancer; cirrhosis; neurological disorder; stroke; Alzheimer* disease; multiple sclerosis; mental retardation; cardiovascular disease; atherosclerosis; angina pectoris; indigestion; congestive heart failure; gastrointestinal disorder; dysphagia; AIDS; gastritis; autoimmune disorder; inflammatory disorder; Crohn's disease; systemic lupus erythematosus; metabolic disorder; diabetes; obesity; viral infection; herpesvirus; parvovirus;
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                                                       Human G-coupled receptor (GCREC) cDNA, Seg ID No 42
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Au-Young J;
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02-JUN-2000; 2000US-0208834F
02-JUN-2000; 2000US-020861F
07-JUN-2000; 2000US-020868F
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Kallick DA, Gandhi AR, Au
                14-MAR-2002 (first entry)
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Best Local Similarity:
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US-10-081-775-2 (1-329) x ABK16633 (1-966)

S

ABK16633 standard; cDNA; 966 BP.

ABK16633

ABK16633

Proposer K

The invention relates to olfactory and Pheromone G-protein coupled receptor (GPCR) or a protein 95% identical to the GPCR, a specific active receptor (GPCR) or a protein 95% identical to the GPCR, a specific active portion and its encoding polynucleotide. Also included are an agonist, antagonist or inhibitor of the GPCR or the polynucleotide, a vector comprising the polynucleotide, a cell transformed by the vector, a noncomprising the polynucleotide of comprising a partial or total deletion of the polynucleotide encoding the receptor and screening (detection and possibly, recovering) of compounds which are known or not known to be agonist, antagonists or inhibitors of natural compounds to the GPCR. The receptor-derived agonists, antagonists, inhibitors or compounds are used as an improvement, elimination or substitution of an existing taste and/or a improvement, elimination or substitution of an existing taste and/or a cused in the preparation of medicament in the treatment and/or prevention used in the preparation of medicament in the treatment and/or prevention of a mammalian disorder, such as cell migration, sterility, psychotic and connection and nerve regeneration for modulating male and female connection and nerve regeneration for modulating male and female connections, hormone production and the menstrual cycle, for the prevention of a promotion and the menstrual cycle, for the prevention of a promotion and the menstrual cycle, for the prevention of a promotion and the menstrual cycle, for the prevention of prevental mammalian. Novel pheromone G-protein coupled receptor and receptor-derived agonists, antagonists or inhibitors useful in food or cosmetic products or in the treatment or prevention of neurological disorders such as anxiety and DNA for olfactory and pheromone G protein-coupled receptor #212 Human; ds; gene; olfactory and pheromone G protein coupled receptor; GPCR; tranquilizer; antidepressant; neuroleptic; endoctine; anabolic; anorectic; trate; fragrance; food additive, cosmetic; cell migration; sterility; psychotic disorder; neurological disorder; anxiety; schizophrenia; manic depression; depression; axonal growth; menstrual cycle; appetite sexual motivation; sexual attraction; Disclosure; Page 646-647; 833pp; English. 21-SEP-2001; 2001WO-BE000162 22-SEP-2000; 2000EP-00870211 WPI; 2002-330013/36. (CHEM-) CHEMCOM SA P-PSDB; AAU95725 #0200224726-A2 schizophrenia Homo sapiens 28-MAR-2002 aggression Veithen A; Human 

behaviours, such as stimulation or suppression of appetite, sexual motivation, sexual attraction, aggression and for promoting or suppressing chemical communication between organisms. The present sequence is a human DNA encoding an olfactory and pheromone GPCR Sequence 966 BP; 182 A; 276 C; 217 G; 291 T; 0 U; 0 Other; Alignment Scores:

prevention or the treatment by stimulation of several mammalian

Conservative: Mismatches: Indels: Length: Matches: 1.34e-164 1649.00 99.07% 98.75% 95.98% Similarity: Percent Similarity: Query Match Best Local

x ABK68612 (1-966) US-10-081-775-2 (1-329)

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BP

ABK68612 standard; DNA; 966

RESULT 10 **ABK68612**  02-JUL-2002 (first entry)

ABK68612

SXXXS

9 28 1 ATGGAATCTCCTAATCACACTGATGTTGACCCTTCTGTCTTCTTCTTCTCTGGGCATCCCA MetGluSerProHisHisThrAspValAspProSerValPhePheLeuLeuGlyIlePro σ

Appendix 137

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Human; gene; anorectic; antiasthmatic; antidiabetic; hypotensive; antiparkinsonian; noctropic; neuroprotective; tranquiliser; antiinflammatory; osteopathic; cardiant; neuroleptic; antiarthritic; gene therapy; olfactory g protein-coupled receptor; GPCR; infection; obesity; diabetes; hypertension; malnutrition; Parkinson's disease; Altheimer's disease; Norsackoff's psychosis; anxiety; rheumatoid arthritis; chronic obstructive pulmonary disease; esteoporosis; asthma; myocardial infarction; schizophrenia; New olfactory G protein-coupled receptor gene nucleic acid and by/ypeptide, useful for diagnosing or treating a disease or condition associated with GPCR, e.g. obesity, diabetes, hypertension, malnutrition or Alzheimer's disease. Human G protein coupled receptor coding sequence SEQ ID 205 24-JUN-2002; 2002WO-IB002481. Martinez RAM, Sigurdsson GT; 26-JUN-2001; 2001US-0301095P, 06-NOV-2001; 2001US-0332758P, (DECO-) DECODE GENETICS EHF WPI; 2003-175284/17. osteoarthritis; ds P-PSDB; ABR01673 WO2003000735-A2 03-JAN-2003 Homo 

The present invention relates to novel human olfactory G protein-coupled receptors (GPCR) and their coding sequences (AB777872-AB277986 and ABR01571-ABR01685). The GPCRs and coding sequences are useful for diagnosing or treating a disease or condition associated with GPCR, e.g. infections, obesity, diabetes, hypertension, maintrition, Parkinson's disease, Alzheimer's disease, Korsakoff's spsychosis, anxiety, rheumatoid arthritis, chronic obstructive pulmonary disease, osteoporosis, asthma, myocardial infarction, schizophrenia, or osteoarthritis Claim 1; Page 103; 383pp; English.

Sequence 948 BP; 174 A; 266 C; 202 G; 306 T; 0 U; 0 Other;

AspLeuAlaAlaSerValSerThrValProLysLeuLeuAla1lePheTrpCysGlyAla 99 147 207 SerValPhePheLeuLeuGlylleProGlyLeuGluGlnPheHisLeuTrpLeuSerLeu 39 59 79 40 ProvalCysGlyLeuGlyThrAlaThrIleValGlyAsnIleThrIleLeuValValVal 88 TIGITGITGITGITICTITCCACAATHGIGGGCAATATAACTATTCTGGTTGTTGTT AlaThrGluProValLeuHisLysProValTyrLeuPheLeuCysMetLeuSerThrlle GCCACTGAACCAGTCTTGCACAAGCCTGTGTACCTTTTTCTGTGCATGCTCTCTAACCATC Length:
Matches:
Conservative:
Mismatches:
Indels: Gaps: US-10-081-775-2 (1-329) x ABZ77974 (1-948) 1.01e-135 1376.00 94.16% 91.75% Percent Similarity: Best Local Similarity: Query Match: Alignment Scores: 20 148 80 셤 ò 요 g ð ઠ

208

ABZ77974 standard; DNA; 948

(first entry)

17-APR-2003

ABZ77974;